UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/546,143	04/10/2000	Peter Karl Matzinger	9473	2653

151 7590 04/08/2003

HOFFMANN-LA ROCHE INC.
PATENT LAW DEPARTMENT
340 KINGSLAND STREET
NUTLEY, NJ 07110

EXAMINER
TRUONG, TAMTHOM NGO

ART UNIT	PAPER NUMBER
1624	18

DATE MAILED: 04/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

UNITED STATES PATENT AND TRADEMARK OFFICE

COMMISSIONER FOR PATENTS
UNITED STATES PATENT AND TRADEMARK OFFICE
WASHINGTON, D.C. 20231
www.uspto.gov

BEFORE THE BOARD OF PATENT APPEALS

AND INTERFERENCES

Paper No. 14

Application Number: 09/546,143
Filing Date: April 10, 2000
Appellant(s): MATZINGER ET AL.

Aaron F. Dubberley

For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 10-12-01.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

Appellant's brief includes a statement that claims 10-27 do not stand or fall together and provides reasons as set forth in 37 CFR 1.192©(7) and ©(8).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

5,583,222 **BARBIER et. al.** 12-1996

Adams, C.P. et. al. "Total Synthesis of balanol: a potent protein kinase C inhibitor of fungal origin" Jounral of Chemical Society, Perkin Transaction I, 1975, pp. 2355-2362.

Krogsgaard-Larsen P. et. al. "Inhibitors of GABA Uptake. Syntheses and H NMR Spectroscopic Investigations of Guvacine, (3RS, 4SR)-4-hydroxypiperidine-3-carboxylic Acid, and Related Compounds" Acta Chemica Scandinavica B, vol. 32, no. 5 (1978), pp. 327-334.

Wade, G. L. Jr. ORGANIC CHEMISTRY, © 1987, pages 103 and 115, Prentice Hall Inc., Englewood Cliffs, New Jersey (cited as a basic principle for geometric isomerism – not to be construed as a new prior art).

(10) First Ground of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 112

The following is a quotation of the **second** paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 12, 14, 15, 17, 19, 21, 23, and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Said claims recite the limitation of "amino protecting group" which has no description in the specification other than "tert.-butoxycarbonyl" as a sole representative of said group. Thus, one skilled in the art cannot ascertain what other groups can be considered as an "amino protecting group". Therefore, **the metes and bounds** of the invention is indefinite.

The following is a quotation of the **first** paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 12, 14, 15, 17, 19, 21, 23, and 25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for R^4 as a tert-butyl ester, tert-

butyl carboxylate, or tert-butoxycarbonyl, does not reasonably provide enablement for the genera with R^4 as another functional group serving as an "amino protecting group". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The disclosure does not provide guidance as to what functional groups, and/or rings can be considered as an amino protecting group. Its mere statement *"R^4 is a protecting group, preferably a tert.-butoxycarbonyl group"* is insufficient for one skilled in the art to consider what other groups can be an "amino protecting group". In considering enablement, undue experimentation is an important factor. Here, the scope of "amino protecting group" is undoubtedly broad, and the generic teaching for preparation only gears toward one "amino protecting group", namely, tert.-butoxycarbonyl. Thus, regarding other groups, one skilled in the art will have to carry out undue experimentation, as the chemical art is unpredictable. Note, the Federal Circuit has repeatedly held that **"the specification must teach those skilled in the art how to make and use the** *full scope of the claimed invention* **without 'undue experimentation'"** (see **In re Wright**, 999 F. 2d 1557, 1561, 27 U.S.P.Q. 2d 1510, 1513 (Fed. Cir. 1993)). Also, the disclosure does not provide the starting material for R^4, nor a source for an "amino protecting group", and thus, undue experimentation is inevitable for one skilled in the art to make and use compounds with R^4 as a group other than tert.-butoxycarbonyl. See **In re Howarth**, 210 U.S.P.Q 689, 693 regarding insufficient enablement. Note, in said case, the starting material was not disclosed, nor was a source named. The court, then, ruled that "**burden rests upon applicant who** *chooses to rely upon*

general knowledge in the art **to render his disclosure enabling to establish that those of ordinary skill in the art can be expected to possess or know where to obtain this knowledge;...**" Thus, 'no disclosure of starting material' is a sound reason to render a specification with insufficient enablement.

(11) Response to Argument on the above issues of 112/ 1st and 2nd paragraphs for claims 12, 14, 15, 17, 19, 21, 23, and 25

Applicant disputes the indefiniteness of the terms "amino protecting group" for the following reasons:

a. Said terms are well-known in the art;

b. Over 500 US patents recite said terms in their claims.

c. Citing textbook of Green a long with case laws such as: In re Skoll (187 USPQ 481), In re Fuetterer (138 USPQ 217), In re Bowen (181 USPQ 48), In re Robins (166 USPQ 552) to support applicant's position.

d. The definition of R^4 as an "amino protecting group" is a functional language.

e. As for enablement, applicant feels that it is not necessary to teach what is well known in the art.

Despite applicant's argument, the issues of 112/1st and 2nd paragraphs should be upheld for the following reasons:

i. The issue of indefiniteness is not whether one skilled in the art can understand a term (or terms), rather it is the metes and bounds of the invention. In the instant case, the terms "amino protecting group" as defined for R^4 does not clearly define the scope of claims 12, 14, 15, 17, 19, 21, 23, and 25. The disclosure does not describe what functional groups, ring(s) said terms encompass, except tert.-butoxycarbonyl. Therefore, when interpreting the instant claims in light of the specification, one does not have a guidance as to what is claimed (or **not** claimed) by the terms "amino protecting group". Applicant cites the textbook of Green for description of an "amino protecting group". However, **it is still unclear whether the scope of "amino protecting group" includes groups cited by Green, or goes beyond that**. While breadth is not indefiniteness, the claims must particularly point out and **distinctly define the metes and bounds** of the subject matter that will **be protected by the patent grant.**

ii. It is recognized that the terms "amino protecting group" are recited in a lot of US patents. However, usually, said terms are used specifically in a reaction step in a claimed process. When read in light of a process, said terms have a more definite metes and bounds. In the instant case, applicant claims intermediates (i.e., compounds) having "amino protecting group" as a substituent. Because in the specification, there is no description as to what constitutes said group (other than tert.-butoxycarbonyl), the final structure of a claimed intermediate is indeterminate. Therefore, the scope of claims reciting said terms is indefinite.

iii. Case laws cited by applicant are outdated. The most recent case law is (**Genetech Inc. v. Novo Nordisk**, 108 F.3d 1361, 42 USPQ 2d 1001 (Fed. Cir. 1997)), in which the court ruled that relying on the knowledge of one skilled in the art cannot cure the deficiency in enablement. Just because a term is well-known in the art, it does not mean one skilled in the art can prepare any intermediate having any "amino protecting group". Based on what disclosed by applicant, one skilled in the art can only make compounds with R^4 as tert.-butoxycarbonyl. It is true applicant does not have to provide enablement for known processes in the art, but applicant is obligated to provide **enablement in commensurate with the scope of the claims**. In the instant case, because the terms "amino protecting group" have such a broad scope that the enablement for only tert.-butoxycarbonyl does **not sufficiently** guide the skilled chemist in preparing intermediates with other amino protecting groups.

(12) Second Ground of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

The rejection of claim 23 under 35 U.S.C. 102(a) based on **Lamp et. al.** is withdrawn herein in light of applicant's argument.

102(b) – Claims 17, 23, and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by the following references:

a. **Krogsgaard-Larsen et. al.** (Acta Chem. Scan. B, 32 (1978), pp. 327-334): Compounds 12 and 13 on page 328 are embraced by formula VIII in claim 17 with R^3 as lower alkyl, and R^4as an amino protecting group.

b. **Adams et. al.** (J. Chem. Soc. Perkin Trans. I, 1995, pp. 2355-2362): Formula X in claim 23 inherently embraces compound 20 on page 2356. Formula XI in claim 25 inherently embraces compound 21 on page 2357.

102(e) – Claim 25 is rejected under 35 U.S.C. 102(e) as being anticipated by **Barbier et. al.** (US 5,583,222). Formula XI in claim 25 inherently embraces compounds B1-B23 listed on columns 18-21.

(13) Response to Argument on 102(b), and (e) rejections for claims 17, 23, and 25

Applicant disputes that the 102 rejections are improper because said references do not disclose the cis-form of the claimed formulae. Applicant argues that the trans-form is structurally different from the cis-form, and thus, cannot anticipate the cis-form of the claimed formulae.

Applicant's argument is well taken; however, the 102 rejections based on inherency should be upheld for the following reasons:

i. Despite applicant's assertion, cis- and trans- forms of a compound have **similar structures** due to their common cores, and substituents. They only differ in the spatial orientation of their substituents. However, spatial orientation of a compound can flip flop from one form to the other because **bonds are not static**. Anyone skilled in the art would know that if a trans-form of a compound, a cis-form also **exists inevitably**. This is the most fundamental principle in stereo-chemistry. So, if a reference discloses a trans-form, then a cis-form will be inherently embraced.

ii. Regarding claim 17, compound #12 of Krogsgaard-Larsen clearly a **cis**-compound because both the –OH locates on the same side with $-C(O)OCH_3$ just as the claimed formula VIII. It is not a racemic mixture of cis- and trans- as suggested by applicant. The symbol, "(±)", refers to optical isomers of the **cis**-compound. Note, both the –OH and the $-C(O)OCH_3$ can be pointed upward or downward, and still have cis-

configuration. See Wade's ORGANIC CHEMISTRY, pages 103 and 115, as evidence for the basic principle of cis- and trans- configurations (or geometric isomerism).

(14) Third Ground of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 25 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Barbier et. al.** (US 5,583,222). On column 9, Barbier et. al. disclose a group of intermediates represented by formula III which resembles the claimed formula XI since the reference's variable Y can be taken as –NH while the –CO-A corresponds to the instant variable R^1, and R^{16} (represents an "amino protecting group") corresponds to the instant R^4. Furthermore, column 18 lists intermediates B1-B23 which have tert-butyl carboxylate as an amino protecting group (e.g., see intermediate B4). While Barbier et. al. do not disclose the cis-configuration of compounds of formula III or its species, such form is suggested in the racemic mixture of cis- and trans- represented by formula III.

Furthermore, Barbier et. al. recognizes that substituents on the heterocyclic ring can have cis-configuration as well (see column 4, line 30). Therefore, one of the ordinary skill in the art would have been motivated to make the cis-configuration of compounds of formula III because such a configuration had been acknowledged by Barbier et. al. as an alternative to trans-configuration. Thus, at the time of the invention, it would have been obvious to one skilled in the art to make intermediates of formula XI and its species because one skilled in the art can always resolve a racemic mixture of formula III by conventional methods to obtain the cis-form of formula XI claimed herein.

(15) Response to Argument on the 103 rejection for claims 25 and 26

Applicant's argues that the broad genus of the disclosed formula III does not allow one skilled in the art to select the intermediates claimed herein.

Applicant's argument cannot overcome the rejection for the following reasons:

i. Barbier et. al. not only disclose the genus of formula III, but also its species (B1-B23). So, one cannot dispute the teaching of Barbier et. al. as merely being broad.

ii. Because the disclosed species B1-B23 are in trans-form, formula III was cited in the rejection as a racemic mixture, which suggests that a cis-form is also implicitly suggested. Therefore, it is within the level of one skilled in the art to obtain the claimed cis-form from the teaching of Barbier et. al., and conventional methods of resolving cis- and trans- forms.

For the above reasons, it is believed that all rejections should be sustained.

Respectfully submitted,

Tamthom N. Truong

March 27, 2003

JOHN M. FORD
PRIMARY EXAMINER
GROUP - ART UNIT 1624

SUPERVISORY PATENT EXAMINER
ART UNIT 1624

RICHARD L. RAYMOND
PRIMARY EXAMINER
ART UNIT 1624

ALAN L. ROTMAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600